REMARKS

In response to the Office Action mailed March 23, 2009 ("Office Action"), Applicant cancels claims 12, 14 and 16, amends claims 1, 10, 13, and 54 and adds new claims 60-63. Support for the claim amendments and new claims is found in the specification as filed, including paragraphs [0018]-[0019], [0118], and [0186]-[0187] of corresponding published US patent application no. US2005/0238870A1. No new matter is added. Claims 1-4, 6-11, 13, 15, 17, 19-31, 49-54, and 56-63 are pending.

Claim Rejections Under 35 U.S.C. § 103(a) (Jacobsen/Greene/Smith)

The Examiner rejected independent claims 1 and 54, along with dependent claims 2, 8, 9, 15, 17, 19-23, 25, 26, 28-31, 49-53, and 56-59 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Jacobsen et al., US 6,530,943 ("Jacobsen") and Greene et al., US 2002/0177855 ("Greene"), in view of Smith et al., US 5,888,930 ("Smith") (Office Action at pages 3-9). The rejected claims cover compositions that include particle chains having at least two connected particles and a link that connects the at least two connected particles. The particle chain also includes at least one of the following: a link having an aspect ratio of at least about 0.001 and at most about 1,000 or a ratio of the diameter of one of the at least two particles to a width of the link of at least about 0.5 and at most about 100. At least one of the at least two connected particles has an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region. Certain dependent claims cover compositions where the two connected particles and the link are formed from the same polymer, where a first particle is attached to two or more particle chains, or a particle has a sphericity of about 0.9 or more.

Jacobsen and Greene describe chains of joined beads (Jacobsen, e.g., col. 2, lines 35-38) or embolizing elements along a filament (Greene, e.g., paragraph [0016]). Jacobsen emphasizes the importance of joining beads having a "central bore," and formed of a material having a

particular density and surface porosity (Jacobsen, e.g., col. 4, lines 28-53).[1] The joined embolizing elements described in Greene are formed from a polymer with sufficient softness to be "coaxially skewered" along a carrier filament, or the embolizing elements are molded around the carrier filament (Greene, e.g., paragraphs [0016] and [0021] - [0024]).[2] Smith describes porous beads having very specific pore structures formed by precipitation methods that require certain specific combinations of solvents, non-solvent liquids and polymers (e.g., Smith at col. 3, lines 6-67; col. 5, lines 13-27).[3] Smith notably fails to disclose how to form such particles having the "central bore" and density requirements emphasized by Jacobsen, or the softness to permit "coaxial skewering" along a filament in the manner disclosed in Greene.

The Office Action appears to take the position that one skilled in the art would join the beads without a central bore from Smith based on Jacobsen and/or Greene to arrive at the claimed composition of connected particles. The Office Action asserts that "one skilled in the art would be capable of providing [a central bore]…" to the particles of Smith by "skewering as taught by Greene" in order to join the particles as disclosed in Jacobsen (Office Action at page 8). Applicants respectfully disagree. The cited references, alone or in combination, do not disclose or render obvious joining the beads of Smith according to the teachings of Greene or Jacobsen, nor do Greene or Jacobsen disclose or render obvious the modification of the particles produced in Smith to obtain the claimed compositions.

---

[1] Jacobsen describes the importance of "selecting the material of the beads… [to] control the density of the string" to have beads that are less than the density of blood (Jacobsen, col. 4, lines 28-32) and having a surface porosity "to promote thrombogenicity" after implantation (Jacobsen, col. 4, lines 48-53). The beads of Jacobsen are formed with a "central bore" through which a filament is "threaded to maintain the beads connected together in a chain" (Jacobsen, col. 9, line 66 – col. 10, line 1).

[2] Greene discloses embolizing elements along the length of a filamentous carrier where formed by "coaxially skewering" softened embolizing elements along the carrier, or disposing a filamentous carrier in a mold followed by transferring polymer under pressure around the carrier in the mold (e.g., Greene, paragraphs [0016] and [0021] through [0024]).

[3] According to Smith, "[i]n order to achieve the continuously-grated pore structure of the beads of the present invention, the polymer, its solvent and the precipitation bath must all be specified" (Smith at col. 3, lines 49-51, emphasis provided); the solvent "must dissolve the polymer and be miscible with the liquid, typically water, used for precipitation" (Smith at col. 3, lines 3-5); the polymer "must be soluble in a suitable solvent and insoluble in a liquid that is miscible with the solvent (Smith at col. 2, line 67 – col. 3, line 1); the rate of solvent exchange with the liquid must be kept slow following a rapid initial precipitation (Smith at col. 3, lines 8-10); and the polymer solution may only contain a liquid nonsolvent in amounts "that the polymer does not begin to precipitate, but remains completely dissolved" (Smith at col. 4, lines 38-42).

The assertions in the Office Action do not support a *prima facie* basis for obviousness (MPEP 2142). The Office Action states that one skilled in the art "would be capable of providing [a central bore]" to the particles from Smith, and alleges that the Applicant has not provided evidence to indicate that "the particles of Smith would make them unsuitable for use as beads in the device of [Jacobsen]" (Office Action at page 8). The Office Action also appears to take the position that one skilled in the art would select those particles (if any) produced by Smith having the pore density and surface porosity requirements described by Jacobsen because Jacobsen discloses "a range of densities to be desirable… and that density can be varied to suit a desired function" (Office Action at page 8).[4] Applicants respectfully note that the Examiner bears the initial burden of factually supporting any asserted *prima facie* basis for obviousness, and that "if the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness" (MPEP 2142). The Office Action does not assert a basis for one skilled in the art to identify those polymer particles (if any) disclosed in Smith that are suitable for preparing the devices in Jacobsen.

Furthermore, this obviousness rejection is improper because the asserted combination of Jacobsen, Smith and Greene do not enable the claimed particle chains having a particle with a mean pore size in an interior region greater than the mean pore size in a surface region. Applicable case law clearly states that "[i]n order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." *Beakman Instruments, Inc. v. LKB Produkter AB,* 892 F2d 1547, 1551, 13 USPQ2d 1301, 1304 (Fed. Cir. 1989). A claim rejection for obviousness under 35 U.S.C. §103 is improper if the person of ordinary skill in the art would not be able to make a claimed composition or perform a claimed method upon reviewing the cited prior art without undue experimentation:

---

[4] Here, the Office Action cites a portion of Jacobsen (col. 4, lines 30-33) stating that beads with a density greater than blood can be made when metals are included in the beads. However, the particles from Smith are made without metals by precipitating a polymer solution (See, e.g., Smith at col. 3, lines 60-67). The Office Action does not provide a reason why one skilled in the art would select those particles (if any) produced by Smith having the pore density and surface porosity requirements described by Jacobsen.

> [r]eferences relied upon to support a rejection under 35 U.S.C. 103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public. [citations omitted] An invention is not 'possessed' absent some known or obvious way to make it." *In re Payne, Durden and Weiden*, 606 F2d 303, 314, 203 USPQ 245, 255 (CCPA 1979).

Under this standard, an obviousness rejection under 35 U.S.C. 103 of a composition claim is improper in "the absence of a known or obvious process for making the claimed compounds." *In re Hoeksema*, 399 F2d 209, 274, 158 USPQ 596, 601 (CCPA 1968).

In this case, the obviousness rejection based on Smith, Jacobsen and/or Greene is improper under this applicable legal standard because one skilled in the art cannot make the compositions in the rejected claims based on the cited prior art, and the Examiner provides no basis to actually make the claimed connected porous particles. Undue experimentation would be required to make and use the claimed connected particles based on the asserted combination of Jacobsen, Smith and Greene. For example, the Office Action provides no explanation how these references, alone or in combination, describe how to: (1) place a "central bore" in each bead produced by the method of Smith (as disclosed by Jacobsen), (2) select those particles (if any) produced by Smith having the pore density and surface porosity requirements described by Jacobsen, and/or (3) provide beads by the process of Smith having a softness adequate to permit joining the particles with the filamentous carrier as described by Greene.

In addition, various dependent claims recite additional features that are even more removed from the disclosures of Jacobsen, Smith and/or Greene. For example, Jacobsen, Smith and/or Greene do not disclose or render obvious a particle chain of at least one of the at least two connected particles comprising the same polymer with a first particle having a sphericity of about 0.9 or more and the first particle attached to two or more particle chains.

Notwithstanding the arguments above, Applicants have elected to amend independent claims 1 and 54 to include limitations from original claims 10 or 12 relating to the aspect ratio of the link or limitations from original claims 13 or 14 relating to the ratio of the diameter of a

particle and a link. Claims 10 and 12-14 were not rejected for obviousness over the combination of Jacobsen, Smith and Greene. Reconsideration and withdrawal of this rejection is requested.

Claim Rejections Under 35 U.S.C. § 103(a) (Jacobsen/Greene/Smith/Mazzocchi)

The Examiner rejected independent claims 1 and 54, along with dependent claims 2-4, 6-15, 17, 19-26, 28-31, 49-53, and 56-59 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Jacobsen, Greene and Smith (discussed above) in further view of US 6,605,102 ("Mazzocchi") (Office Action at page 9).

For the reasons noted above, the combination of Jacobsen, Greene and Smith does not render the subject matter covered by claims 1-4, 6-15, 17, 19-26, 28-31, 49-54 and 56-59 unpatentable under 35 U.S.C. § 103(a). Mazzocchi does not cure the deficiencies of these references. The Office Action asserts that "the disclosure of Mazzocchi is not limited to a filter" and that it "would have been obvious… to selectively prepare links within the claimed ranges, which would be directly related to aspect ratio…" (Office Action at page 13). Applicants respectfully disagree. Mazzocchi fails to disclose or render obvious particles joined by a link having an aspect ratio of at least 0.001 and an aspect ratio of at most 1,000, where the aspect ratio is the ratio of the length of the link to the width of the link (e.g., paragraph [0123] of the present application, published as US2005/0238870A1).[5] Mazzocchi fails to disclose or render obvious particles joined by a link having the claimed aspect ratios.[6]

Furthermore, the Office Action does not explain how Mazzocchi, alone or in combination with Jacobsen, Greene and/or Smith, discloses or renders obvious joined particles with the ratio of the diameter of one particle to the width of a link joining the

[5] Mazzocchi discloses devices for "filtering embolic particles from blood," but does not disclose or render obvious particle chains (*See, e.g.,* Mazzocchi, col. 21, lines 5-23).

[6] Mazzocchi describes filters to remove embolic particles from a blood vessel (e.g., Mazzocchi at col. 19, lines 53-64). In particular, Mazzocchi describes resiliently expandable tubular metal fabric devices forming a bell-shaped fabric disc oriented perpendicular to the axis of the metal fabric tube. These devices are used to form a temporary filter deployed to trap embolic particles within a body channel (e.g., Mazzocchi at col. 2, line 53 – col. 3, line 29 and col. 19, lines 53-64). Mazzocchi also discloses devices with an entirely different aspect ratio. Mazzocchi describes an aspect ratio of "the ratio of the length of the device over its minimum diameter or width," which is desirably at least about 1.0 and preferably about 1.0 to 3.0 (Mazzocchi at col. 11, lines 59-63, emphasis added).

particles being at most about 100 and at least about 0.001. The Office Action appears to take the position that since "Jacobsen teaches that the carriers may be any desired length," it would thus have been obvious to one skilled in the art "to selectively prepare links within the claimed ranges" (Office Action at page 13). However, "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness" (MPEP 2142, citations omitted). Here, the Office Action provides no basis in Jacobsen or elsewhere to make compositions with the particular links covered by claims 1-4, 6-15, 17, 19-26, 28-31, 49-54 and 56-59. In addition, various dependent claims recite additional features that are even more removed from the disclosures of Mazzocchi, Jacobsen, Greene and/or Smith. For example, Mazzocchi, Jacobsen, Greene and/or Smith do not disclose or render obvious a particle chain of at least one of the at least two connected particles comprising the same polymer with a first particle having a sphericity of about 0.9 or more and the first particle attached to two or more particle chains.

Applicants request reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 103(a) (Jacobsen/Mangin)

The Examiner rejected independent claims 1 and 54 with dependent claims 2-7, 15, 17, 19, 21, 22, 25-31, 49-53, and 56-59 under 35 U.S.C. § 103(a) as being unpatentable over Jacobsen in view of Mangin, WO 01/66016 ("Mangin") (Office Action at pages 13-23). As discussed above, Jacobsen discloses a chain of particles having a central bore and a particular density. Mangin discloses unconnected embolic particles having voids present within the particles as well as on the surface of the particles, where the surface region has both large pores and small pores (e.g., Mangin, FIG. A), and the interior region also has both large pores and small pores (e.g., FIG. B). However, neither Jacobsen nor Mangin, either alone or in combination, discloses or renders obvious such particle chains

In response to Applicant's arguments, the Examiner states:

> [a] single figure depicting a cross-section of a particle can be sufficient to demonstrate pore size distribution. This interpretation is supported by the instant specification, which shows only a cartoon of a single cross section, see Figure 5 of the instant Application (Office Action at page 17)

Applicants respectfully disagree. Figure 1A is a "schematic diagram showing the structure of an embolic particle" that "comprises voids at the surface" (Mangin at p. 5, lines 34-36). Mangin's Figure 1B is a cross-sectional view of the particle in Figure 1A that includes a two dimensional circular area representing one cross-section of the particle. As one skilled in the art would understand, an "interior region" of a particle is three dimensional and a "surface region" of a particle is two or three dimensional and therefore to obtain features of the surface and interior regions of a particle, more than one cross-sectional view of the particle is required. Accordingly, one would also understand that even though Mangin's Figure B shows that the two dimensional circumference includes pores having larger sizes than the pores in the two dimensional circular area, one cannot conclude that in a three dimensional space, Mangin's particle includes a surface region that has pores with larger mean sizes than the pores in the interior region of the particle. To strictly analyze the distribution of pore sizes in Mangin's particles, infinite numbers of cross-sectional views as shown in Mangin's Figure B are needed. In fact, nowhere does Mangin disclose or otherwise indicate that his particles have an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region, as recited by the rejected claims. Applicants request reconsideration and withdrawal of the rejection of these claims.

Claim Rejections Under 35 U.S.C. § 103(a) (Jacobsen/Lanphere)

The Examiner rejected independent claims 1 and 54, along with dependent claims 2-4, 6, 7, 15, 17, 19-23, 25-31, 49-53, and 56-59 under 35 U.S.C. 103(a) as being obvious over Jacobsen (discussed above) in view of Lanphere et al., US 2003/0185895 ("Lanphere") (Office Action at pages 8-9). For at least the reasons noted above, Jacobsen does not disclose or render obvious the features of claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59. The Office Action maintains that "it would have been obvious… to apply the porous PVA particles taught by

Lanphere in an interconnected form, as taught in the device of Jacobsen, because both the porous particles of Lanphere and the interconnected porous beads of Jacobsen are used for embolization" (Office Action at page 19).

As noted above, Jacobsen describes the importance of "selecting the material of the beads… [to] control the density of the string" to have beads that are less than the density of blood (Jacobsen, col. 4, lines 28-32) and having a surface porosity "to promote thrombogenicity" after implantation (Jacobsen, col. 4, lines 48-53).[7] The beads of Jacobsen are formed with a "central bore" through which a filament is "threaded to maintain the beads connected together in a chain" (Jacobsen, col. 9, line 66 – col. 10, line 1). Jacobsen does not disclose or render obvious particle chain compositions where an interconnected particle has a mean pore size that is greater in a surface region than an interior region. Lanphere does not cure the deficiencies of Jacobsen. Lanphere discloses drug delivery particles that include a reservoir region having primarily larger pores and a metering region (e.g., Lanphere, Abstract). Jacobsen's particles in his particle chain do not include the features of Lanphere's particles. Therefore one skilled in the art would understand that Jacobsen's method of making his particle chains would not be suitable for making particle chains that include Lanphere's particles, and accordingly, one would not know how to make particle chains that include Lanphere's particles. In particular, the Office Action provides no explanation how these references, alone or in combination, describe how to: (1) place a "central bore" in each bead described by Lanphere (as disclosed by Jacobsen) and/or (2) select those particles (if any) produced by Lanphere having the pore density and surface porosity requirements described by Jacobsen.

Thus, neither Jacobsen nor Lanphere, alone or in combination, discloses or renders obvious the subject matter covered by claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59. Accordingly, Applicants seek reconsideration and withdrawal of the rejection of these claims.

---

[7] The Office Action maintains that it would be obvious for one skilled in the art to join the particles of Lanphere because Jacobsen discloses joined particles with "a range of [particle] densities to be desirable" (Office Action at page 22). In support of this assertion, the Office Action cites a portion of Jacobsen (col. 4, lines 30-33) stating that beads with a density greater than blood can be made when metals are included in the beads. Accordingly, Jacobsen discloses that particles with metal can be used to produce densities greater than that of blood. The Office Action does not, however, provide a reason why one skilled in the art would select those particles (if any) produced by Lanphere having the pore density and surface porosity requirements described by Jacobsen.

Notwithstanding the arguments above, Applicants have elected to amend independent claims 1 and 54 to include limitations from original claims 10 or 12 relating to the aspect ratio of the link or limitations from original claims 13 or 14 relating to the ratio of the diameter of a particle and a link. Claims 10 and 12-14 were not rejected for obviousness over the combination of Jacobsen and Lanphere. Reconsideration and withdrawal of this rejection is requested.

Conclusion

Applicants believe the application is now in condition for allowance, which action is requested. Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 01194-0459001.

Respectfully submitted,

Date: May 4, 2009

/Nicholas M. Boivin/
Nicholas M. Boivin
Reg. No. 45,650

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906
22159996.doc